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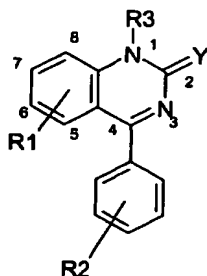
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For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: DERIVATIVES OF ARYL-QUINAZOLINE/ARYL-2-AMINO-PHENYL METHANONE WHICH PROMOTE THE RELEASE OF PARATHYROID HORMONE



(I)

(57) Abstract: A compound of formula (I): wherein R1, R2, R3 and Y are as defined herein, or a pharmaceutically-acceptable and -cleavable ester, or acid addition salt thereof, useful for promoting the release of parathyroid hormone, e.g. for preventing or treating bone conditions which are associated with increased calcium depletion or resorption or in which stimulation of bone formation and calcium fixation in the bone is desirable.

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A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 A61K31/498 C07D403/06 C07D239/82 C07D403/10 C07D409/06
C07D405/06 C07D417/06 C07D401/06 C07D413/06 C07D401/12
C07D239/78 C07C49/84 A61P5/18

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C07D C07C

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, CHEM ABS Data, WPI Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	RUSSELL, R. K. ET AL: "Synthesis and renal vasodilator activity of substituted '4-alkyl(aryl)-2-oxoquinazolin-1-yl'alkanoic acids" EUROPEAN JOURNAL OF MEDICINAL CHEMISTRY, vol. 27, no. 3, 1992, pages 277-284, XP002935850	1,2
A	page 284, left-hand column; examples 30,31	3-8
X	DATABASE CAPLUS 'Online! CHEMICAL ABSTRACTS SERVICE, COLUMBUS, OHIO, US; XP002280288 retrieved from STN accession no. 1306 Database accession no. 1980:121782 rn:73052-29-6 abstract -/-	1,2

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

*** Special categories of cited documents:**

- *A* document defining the general state of the art which is not considered to be of particular relevance
- *E* earlier document but published on or after the international filing date
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- *O* document referring to an oral disclosure, use, exhibition or other means
- *P* document published prior to the international filing date but later than the priority date claimed

- *T* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- *X* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- *Y* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- *Z* document member of the same patent family

Date of the actual completion of the international search

8 June 2004

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18/06/2004

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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
	& MIYAGISHI, AKIRA ET ALL: "General pharmaceutical studies on ciproquazone (SL-573) and its metabolites" OYO YAKURI, vol. 18, no. 1, 1979, pages 9-22,	
X	MASAI, NARUHITO ET AL: "Carbon-13 nuclear magnetic resonance studies of anti-inflammatory 2(1H)-quinazolinones" CHEMICAL & PHARMACEUTICAL BULLETIN, vol. 25, no. 11, 1977, pages 3018-3022, XP009000437 examples 3,4,6-10,12	1,2
X	DATABASE CAPLUS 'Online! CHEMICAL ABSTRACTS SERVICE, COLUMBUS, OHIO, US; XP002280289 retrieved from STN accession no. 1406 Database accession no. 1982:503745 rn:37554-38-4 abstract & S. MARDENTE, C. BICCHI, M.G.NANO: "GLC-ECD determination of 1-(2-hydroxyethyl)-3-hydroxy-7-chloro-1,3-dihydro-5-(O-fluorophenyl)-2H-1,4-benzodiazepin-2-one (SAS 643) in plasma and urine and identification of its main biotransformation products" THERAPEUTIC DRUG MONITORING, vol. 3, no. 4, 1981, pages 351-356,	1,2
X	US 4 387 223 A (YAMAMOTO MICHIMIRO ET AL) 7 June 1983 (1983-06-07) column 4, lines 5,36	1,2
A	column 2, lines 12-17	5-8
X	CH 612 186 A (SUMITOMO CHEMICAL CO) 13 July 1979 (1979-07-13) page 4, left-hand column, lines 1,7,32; claim 1	1,2
X	US 3 812 257 A (INAHARA S ET AL) 21 May 1974 (1974-05-21) column 9, lines 10-70	1,2
A	column 3, line 67 column 4, lines 1,3,6,52	3-8
X	GB 1 353 789 A (SUMITOMO CHEMICAL CO) 22 May 1974 (1974-05-22) page 2, left-hand column, lines 25-39 page 4, right-hand column, lines 68,71,74 page 5, lines 47,76,82	1,2
A		3-8
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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	<p>DATABASE CAPLUS 'Online! CHEMICAL ABSTRACTS SERVICE, COLUMBUS, OHIO, US; XP002280290 retrieved from STN accession no. 1142 Database accession no. 1994:244939 rn:154374-68-2P; 154374-67-1 abstract & M.I. JAEDA AT ALL: "Synthesis of some novel 2(1H)-quinazolinones and 2-thioxo analogs from newly synthesized 1-acyl-3-alkoxyphenylureas and tioureas" JOURNAL OF CHEMICAL TECHNOLOGY AND BIOTECHNOLOGY, vol. 58, no. 4, 1993, pages 391-394,</p>	1,2
X	<p>US 5 773 663 A (REHNIG ANNEROSE EDITH ELISE ET AL) 30 June 1998 (1998-06-30) column 36, line 60 - column 40, line 65; example 115 column 1, line 35 - column 2, line 30</p>	3,4
A		1,2,5-8
X	<p>US 5 856 503 A (MAERKI HANS-PETER ET AL) 5 January 1999 (1999-01-05) column 16, line 53 - column 20, line 45; example 35</p>	3,4
A		1,2,4-8
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X	<p>DATABASE CROSSFIRE BEILSTEIN 'Online! Beilstein Institut zur Förderung der Chemischen Wissenschaften, Frankfurt am Main, DE; XP002280292 Database accession no. 6810088 abstract & B.BERGER, M.BOLTE: ACTA CRYSTALLOGR. SECT.C: CRYST. STRUCT. COMMUN, vol. 50, 1994, pages 773-775,</p>	3,4
A	<p>US 3 925 548 A (HANS OH, PFEFFINGEN) 9 December 1975 (1975-12-09) column 10, line 52 - column 12, line 15; claims; examples 9,15</p>	1-8
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International Application No

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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	WO 02/24683 A (JANSSEN PHARMACEUTICA NV ;ANGIBAUD PATRICK RENE (FR); VENET MARC G) 28 March 2002 (2002-03-28) page 72-compounds 'B6!', 'B20! page 77, lines 2-12; claims	1-8
A	US 6 211 244 B1 (DELMAR ERIC G ET AL) 3 April 2001 (2001-04-03) claims; figures	1-8
P,X	WO 02/102782 A (NOVARTIS AG, SWITZ.;NOVARTIS-ERFINDUNGEN VERWALTUNGSGESELLSCHAFT M.B.H) 27 December 2002 (2002-12-27) the whole document	1-4

INTERNATIONAL SEARCH REPORT

International application No.
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Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:
Although claim 7 is directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.
2. ☒ Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
see FURTHER INFORMATION sheet PCT/ISA/210
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this International application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.1

Although claim 7 is directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.

Continuation of Box I.2

Claims Nos.: -

Present Claims 1 and 3 relate to an extremely large number of possible compounds. In fact, Claims 1 and 3 contain so many options, variables, possible permutations that a lack of clarity (and conciseness) within the meaning of Article 6 PCT and/or disclosure within the meaning of Article 5 PCT arises to such an extent as to render a meaningful search of the above-mentioned claims impossible. The claims 1 and 3 can in no way be considered to be a reasonable generalisation of the actual examples since it include numerous possibilities which cannot be considered as equivalents, homologues or analogues of the examples. Consequently, the search was carried out for those parts of the application which do appear to be clear (concise and supported by the examples), namely for the compounds for which R1 is a 2-propynyloxy, methoxy or hydroxy moiety and R3 is an optionally substituted alkyl, alkenyl or benzyl. All the examples have been searched.

The applicant's attention is drawn to the fact that claims relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure. If the application proceeds into the regional phase before the EPO, the applicant is reminded that a search may be carried out during examination before the EPO (see EPO Guideline C-VI, 8.5), should the problems which led to the Article 17(2) declaration be overcome.

INTERNATIONAL SEARCH REPORT

Information on patent family members

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